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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,096	12/30/2003	Doddabele L. Madhavi	BIO 2-013	6934

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EXAMINER	
FEDOWITZ, MATTHEW L	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 10/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/748,096	MADHAVI ET AL.	
	Examiner	Art Unit	
	Matthew L. Fedowitz	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☒ Claim(s) *5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Priority

Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(e) to the provisional application 60/468378 filed May 6, 2003.

It is noted that this application appears to claim subject matter disclosed in prior copending Application No. 60/468378, filed May 6, 2003. A reference to the prior application must be inserted as the first sentence of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). Also, the current status of all non-provisional parent applications referenced should be included.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Objections

Claim 5 is objected to because it depends from itself. Claim 5 is examined as if it depended from anyone of claims 1-4. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10-17 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 provides a method of treating an animal with a bioavailable coenzyme Q-10 complex, but, since the claim is not directed toward a particular disease state, it is unclear what method/process applicant is intending to encompass. As a result, claim 10 is rendered to be indefinite. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims depending from a base claim that fail to obviate the reason said base claim is rejected for indefiniteness, are also rejected for the reasons of record. Claims 11-17 are rejected under the second paragraph of 35 U.S.C. § 112.

Claim Rejections - 35 USC § 102

The following is a quotation of 35 U.S.C. § 102(b) that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 5 (as dependent from claim 1), 6, and 9 are rejected under 35 U.S.C. § 102(b) as being anticipated by Iijima *et al.* (JP 57-157912).

A. Claim 1 teaches a water-dispersible, freeze-dried bioavailable coenzyme Q-10/ cyclodextrin complex. Iijima *et al.* teach a water dispersible freeze-dried bioavailable coenzyme Q-10/ cyclodextrin complex (see page 9 column 1 bracketed section, page 10 columns 3 – 4 bracketed section and page 12 column 11 bracketed section).

B. Claim 4 teaches the complex of claim 1 where the cyclodextrin consists of β-cyclodextrin or γ-cyclodextrin. Iijima *et al.* teach the complex of β-cyclodextrin and coenzyme Q-10 (see page 9 column 1 bracketed section).

C. Claim 5 recites a complex interpreted to be depending from anyone of claims 1-4 which is formulated into one or more of a topical preparation, a sublingual formulation, or for oral ingestion. Iijima *et al.* teaches an oral and injectable bioavailable form of the coenzyme q-10/cyclodextrin complex (see page 10 column 3 bracketed section). The claim for "a sublingual formulation, or for oral ingestion" is redundant because a

sublingual formulation is administered by the mouth and an oral formulation is administered by the mouth and both are anticipated by *Iijima et al.*

D. Claim 6 teaches a method for making a water-dispersible complex, which comprises the steps of preparing a slurry of coenzyme Q-10 and cyclodextrin then drying the formulation by spray, vacuum or freeze drying. Iijima *et al.* teaches a method for making the coenzyme Q-10/cyclodextrin complex that includes air and freeze-drying the aqueous compound to yield a dried complex (see page 12 column 11 bracketed section).

E. Claim 9 teaches that the cyclodextrin of claim 6 is β-cyclodextrin. Iijima et al. teach that the method for making the water-dispersible complex uses β-cyclodextrin (see page 12 column 11 bracketed section).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1) Determining the scope and contents of the prior art.
2) Ascertaining the differences between the prior art and the claims at issue.
3) Resolving the level of ordinary skill in the pertinent art.
4) Considering objective evidence present in the application indicating obviousness or nonobviousness.

A. Claims 2, 3 and 4, are rejected under 35 U.S.C. § 103(a) as being unpatentable over Patel *et al.* (US 6,569,463), Iijima *et al.* (JP 59-047202 A) and Miyao *et al.* (JP 60-089442).

Claims 2, 3 and 4 are directed to a water-dispersible, freeze-dried bioavailable coenzyme Q-10/cyclodextrin complex wherein the formulation consists of molar ranges from about 0.5:1 to 10:1 and 1:1 to 2:1 of coenzyme Q-10/cyclodextrin respectively that make use of β-cyclodextrin or γ-cyclodextrin.

Patel *et al.* teach a water-dispersible (see column 46 line 64 through column 49 line 34) freeze-dried (see column 40 lines 10-18) bioavailable (see column 2 lines 36-39) coenzyme Q-10/cyclodextrin complex (see column 28 lines 20-48) for improved delivery

of hydrophobic active ingredients in pharmaceutical compositions. Patel *et al.* does not teach specific ratios of coenzyme Q-10 to cyclodextrin in creating a formulation. Patel *et al.* also does not teach the use of β-cyclodextrin or γ-cyclodextrin. Iijima *et al.* does teach formulations consisting of coenzyme Q-10 and cyclodextrin derivatives (see page 11 column 10 bracketed section) including β-cyclodextrin (see page 9 column 1 bracketed section). In addition, Miyao *et al.* teach a formulation of coenzyme Q-10 and γ-cyclodextrin (see abstract).

Therefore, it would have been obvious to one having ordinary skill in this art at the time the invention was made to prepare formulations of coenzyme Q-10 with cyclodextrin in the ratios of 0.5:1 to 10:1 and 1:1 to 2:1 having the above cited references before him. By considering the teaching of Patel *et al.* regarding a water-dispersible, freeze-dried bioavailable coenzyme Q-10/cyclodextrin complex for improved delivery of hydrophobic active ingredients in pharmaceutical compositions as well as the teaching from Iijima *et al* that a coenzyme Q-10 complex has a heightened solubility and rate of absorption when combined with β-cyclodextrin would lead one skilled in the art to have a reasonable expectation of success in combining Patel *et al.* with Iijima *et al.* to obtain an optimized formulation for a highly bioavailable coenzyme Q-10 and cyclodextrin complex.

In addition, by considering the teaching of Patel *et al.* regarding a water-dispersible, freeze-dried bioavailable coenzyme Q-10/cyclodextrin complex for improved delivery of hydrophobic active ingredients in pharmaceutical compositions as well as the teaching from Miyao *et al.* of the use of γ-cyclodextrin would lead one skilled in the art

to have a reasonable expectation of success in combining Patel *et al.* with Miyao *et al.* to obtain an optimized formulation for a highly bioavailable coenzyme Q-10 cyclodextrin complex.

Patel *et al.* provides the motivation to produce "a highly bioavailable coenzyme Q-10 and cyclodextrin complex" because due to the lipophilic nature, low bioavailability and therapeutic use of coenzyme Q-10 a need arises to enhance the delivery of hydrophobic active ingredients (see US 6,569,463 abstract).

B. Claims 7, 8 and 9 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Patel *et al.* (US 6,569,463), Iijima *et al.* (JP 59-047202 A) and Miyao *et al.* (JP 60-089442).

Claims 7, 8 and 9 are directed to a method for making a water-dispersible complex by combining an aqueous formulation of coenzyme Q-10 and cyclodextrin then spray, vacuum or freeze drying the aqueous formulation to form the complex wherein the formulation consists of molar ranges from about 0.5:1 to 10:1 and 1:1 to 2:1 of coenzyme Q-10/cyclodextrin respectively that make use of either β-cyclodextrin or γ-cyclodextrin.

Iijima *et al.* teach a method for making the coenzyme Q-10/cyclodextrin complex that includes air and freeze-drying the aqueous compound to yield a dried complex (see page 12 column 11 bracketed section) as well as the use of β-cyclodextrin (see page 9 column 1 bracketed section). Iijima *et al.* also teach formulations consisting of coenzyme Q-10 and cyclodextrin derivatives that have heightened solubility and absorption rates (see page 11 column 10 bracketed section). Iijima *et al.* does not teach a water

dispersible complex or the use of γ-cyclodextrin in complex with coenzyme Q-10. However, Patel *et al.* does teach a water dispersible complex (see column 46 line 64 through column 49 line 34) and Miyao *et al.* does teach a formulation of coenzyme Q-10 and γ-cyclodextrin (see abstract).

Therefore, it would have been obvious to one having ordinary skill in this art at the time the invention was made to prepare formulations of coenzyme Q-10 with cyclodextrin in the ratios of 0.5:1 to 10:1 and 1:1 to 2:1 having the above cited references before him. By considering the teachings of Iijima *et al.* regarding a method for making the coenzyme Q-10/cyclodextrin complex that includes air and freeze-drying the aqueous compound to yield a dried complex and the use of β-cyclodextrin in coenzyme Q-10 formulations to yield heightened solubility and absorption rates with the teaching of Patel et al. regarding the use of a water-dispersible complex would lead one skilled in the art to have a reasonable expectation of success in combining Iijima *et al.* with Patel *et al.* to obtain an optimized formulation for a highly bioavailable coenzyme Q-10/ cyclodextrin complex.

In addition, by considering the teachings of Iijima *et al.* regarding a method for making the coenzyme Q-10/cyclodextrin complex that includes air and freeze-drying the aqueous compound to yield a dried complex as well as the teaching from Miyao *et al.* of the use of γ-cyclodextrin would lead one skilled in the art to have a reasonable expectation of success in combining Iijima *et al.* with Miyao *et al.* to obtain an optimized formulation for a highly bioavailable coenzyme Q-10 and cyclodextrin complex.

Patel *et al.* provides the motivation to produce "a highly bioavailable coenzyme Q-10 and cyclodextrin complex" because due to the lipophilic nature, low bioavailability and therapeutic use of coenzyme Q-10 a need arises to enhance the delivery of hydrophobic active ingredients (see US 6,569,463 abstract).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Matthew L. Fedowitz whose telephone number is (571) 272-3105. The examiner can normally be reached on 9am-5:30pm (EST) M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Matthew L. Fedowitz, Pharm.D., Esq.
October 13, 2004

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Art Unit 1623